**Objective**

To determine whether first trimester biomarkers of placental function can be used to screen for spontaneous preterm birth (sPTB) and develop prediction models with maternal factors, obstetric history and biomarkers of placental function at 11-13 weeks for the calculation of patient-specific risks for sPTB.

**Methods**

This was a secondary analysis of the data derived from a prospective cohort study for first trimester screening for preeclampsia in singleton pregnancies at 11-13+6 weeks’ gestation in women attending for routine Down syndrome screening at a tertiary obstetric unit between December 2016 to December 2019. A split-sample internal validation method was adopted to explore and develop prediction models for all sPTB at <37 weeks and those with preterm prelabor rupture of membranes (PPROM) using maternal risk factors, uterine artery Doppler indices, serum placental growth factor (PlGF), pregnancy associated plasma protein-A (PAPP-A), and beta human chorionic gonadotropin (hCG). Screening performance was assessed by receiver operating characteristic (ROC) curve analysis with the areas under the ROC curves (AUC) calculated.

**Results**

A total of 9,298 singleton pregnancies were included in this study. Spontaneous preterm delivery at <37 weeks and <34 weeks occurred in 362 cases (3.89%) including 231 cases (2.48%) of PPROM, and 87 cases (0.94%) including 39 cases (0.42%) of PPROM, respectively. Identified maternal risk factors for sPTB at <37 weeks included chronic hypertension, conception by in-vitro fertilization and history of prior PTB; whereas for PPROM at <37 weeks included conception by in-vitro fertilization and history of prior PTB. The median PlGF multiple of median (MoM) and PAPP-A MoM were significantly reduced in women who had sPTB at <37 weeks as well as in those who had PPROM, compared to those who delivered at term. Screening with a combination of maternal risk factors and PAPP-A/PlGF achieved better performance in predicting sPTB at <37 weeks (AUC 0.630 vs 0.555, detection rate (DR) 24.8% vs 16.6% at false positive rate (FPR) of 10%, p=<0.0001) and PPROM at <37 weeks (AUC 0.643 vs 0.558, DR 28.1% vs 17.0% at FPR of 10%, p=<0.0001) than using maternal risk factors alone. Both models were successfully applied to the internal validation dataset, with AUC of 0.628 and 0.650, respectively.

**Conclusion**

We have demonstrated that low levels of maternal serum PAPP-A and PlGF in the first trimester are associated with increased risks of sPTB and PPROM. However, further research is needed to identify additional biomarkers to improve the screening performance of the combined model using maternal risk factors and PAPP-A/PlGF before clinical application.